201-16299A

HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN
FOR
C. I. Pigment Red 49 (Barium)
(CAS NO.:1103-38-4)

PREPARED BY:
COLOR PIGMENTS MANUFACTURERS ASSOCIATION, INC.
MONOAZO AND RELATED PIGMENTS COMMITTEE

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OVERVIEW

The Monoazo and Related Pigments Committee ("MRPC") of the Color Pigment Manufacturers Association, Inc. (CPMA) and its member companies hereby submits for review and public comment the test plan for C.I. Pigment Red 49 (Barium) (CAS NO.:1103-38-4) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge Program. It is the intent of the MRPC and its member companies to use existing data, and predictive computer models to adequately fulfill the Screening Information Data Set (SIDS) for the various physicochemical, environmental fate, ecotoxicity test, and human health effects endpoints.

C.I. Pigment Red 49 (Barium) (CAS NO.:1103-38-4) is a stable solid. This chemical is used to provide color to products in the printing inks, paints and plastic industries. This chemical is stable in neutral solutions, and is considered "not readily biodegradable".

TEST PLAN SUMMARY

CAS No.1103-38-4	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Req.
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA							
Melting Point	Y	-	-	Y	N	Y	N
Boiling Point	N/A	-	-	Y	N	Y	N
Vapor Pressure	Y	-	-	Y	N	Y	N
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	-	-	Y	Y	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	-	Y	N	Y	N
Stability in Water	N\A	Y			-	Y	N
Biodegradation	Y	Y	-	-	Y	Y	N
Transport between Environmental Compartments	Y	Y	-	Y	N	Y	N
(Fugacity)	Y			Y		Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y	-	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y		-	Y	Y	N
Toxicity to Aquatic Plants	Y	Y		-		Y	N
TOXICOLOGICAL DATA							
Acute Toxicity	Y	-	Y	-	-	Y	N
Repeated Dose Toxicity	Y	Y		-	-	Y	N
Genetic Toxicity – Mutation	Y	Y	-	-	-	Y	N
Genetic Toxicity – Chromosomal Aberrations	Y	Y	-	-	-	Y	N
Developmental Toxicity	Y	-	Y	-	-	Y	N
Toxicity to Reproduction	Y	-	Y	-	-	Y	N

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

Melting point -	A value for this endpoint was obtained from a reputable journal and through surrogate data for C.I. Pigment Red 53, published values from reputable journals and estimations.
Boiling Point -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.
Vapor Pressure -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.
Partition Coefficient -	A value for this endpoint was obtained from an estimation analysis of a surrogate substance C.I. Pigment Red 53.
Water Solubility -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN. A value for this endpoint was also obtained from analysis of a surrogate substance C.I. Pigment Red 53.
Conclusion:	All end points have been satisfied by utilizing data obtained from the various physical chemical data modeling programs within EPIWIN or using measured values. The results of the various computer estimation models within EPIWIN have been noted by the Agency as acceptable in lieu of actual data or values identified from textbooks. No new testing is required.

B. Environmental Fate

Photodegradation -	A value for this endpoint was obtained using AOPWIN, a computer estimation-modeling program within EPIWIN (1).
Stability in Water -	A value for this endpoint was obtained from analysis of a surrogate substance C.I. Pigment Red 53
Biodegradation -	This endpoint was satisfied through the use of an OECD-301C test.
Fugacity -	A value for this endpoint was obtained using the EQC Level III partitioning computer estimation model within EPIWIN.
Conclusion:	All endpoints have been filled with data utilizing acceptable methodologies and of sufficient quality to fulfill these endpoints. No new studies are being proposed.

C. Ecotoxicity Data

Acute Toxicity to Fish -	This endpoint is filled by data from a study for the surrogate substance C.I. Pigment Red 53 .
Acute Toxicity to Aquatic Invertebrates -	This endpoint is filled by data from a study that followed OECD TG-202 and was conducted under GLP assurances for the surrogate substance C.I. Pigment Red 53 .
Toxicity to Aquatic Plants	This endpoint is filled by data from an acceptable estimation
Bioaccumulation	This endpoint is filled by data from for the surrogate substance

C.I. Pigment Red 53 .

Conclusion: All endpoints have been satisfied with data from studies that were conducted using established OECD guidelines. In total, these currently available studies are of sufficient quality to conclude that no additional testing is needed.

D. Toxicological Data

Acute Toxicity - This endpoint is filled by oral exposure data from various published and unpublished references to studies completed in 1961, 1968, 1972, 1976, 1985 and 1992 precise information on protocols followed is not available. Nevertheless, given the number of studies and the consistent results this data is considered "reliable with restrictions". Data for Skin sensitization, skin irritation and eye irritation are also available.

Repeat Dose Toxicity - This endpoint is filled by data from a several studies for the surrogate substance C.I. Pigment Red 53 and a long term study.

Genetic Toxicity

Mutation - This endpoint is filled by published values and data from a study that followed OECD TG-471 for the surrogate substance C.I. Pigment Red 53 .

Aberration - This end point is filled by published values supplied by manufacturers and data from a study that followed OECD TG-473 for the surrogate C.I. Pigment Red 53 .

Developmental Toxicity - This endpoint is filled by data from long term feeding studies for the surrogate substance C.I. Pigment Red 53 .

Reproductive Toxicity - This endpoint is filled by data from long term feeding studies for the surrogate substance C.I. Pigment Red 53 .

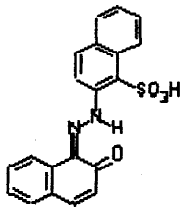
Conclusion: All endpoints have been satisfied with data on C.I. Pigment Red 49 or through the use of structural surrogates, which are of sufficient quality to conclude that no additional testing is needed.

Rationalization for Use of Surrogate Data

As a means to reduce the number of tests that may be conducted the EPA allows for the use of data from structurally similar compounds to characterize specific SIDS endpoints (US EPA 1999a). Accordingly, the MRPC believes that data from the available studies for D & C Red Number 9, C.I. Pigment Red 53 (CAS Numbers 2092-56-0 (Na) and 5160-02-1 (Ba)) meets the needed criteria for use as a surrogate in the completion of some SIDS endpoints. Both color pigments, C.I. Pigment Red 49 and C.I. Pigment Red 53 are derived from 2-Naphthol. As is readily seen by their structures below, C.I. Pigment Red 49 and C.I. Pigment Red 53 are similar compounds sharing the same basic chemical structure. These minor differences do not significantly alter the basic physicochemical properties or the basic biological effects. Both compounds have similar acute toxicity values and predicted characteristics. Accordingly, data from C.I. Pigment Red 53 have been used when necessary to fulfill SIDS endpoints.

Common Name: C.I. Pigment Red 49 Barium,

Structure:

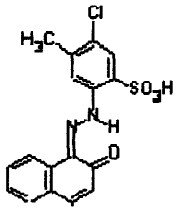


Chemical Name: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-barium

Melting Point:
Boiling Point: Solid
Density 12.3 to 15.8 Pounds Per U.S. Gallon, NPIRI
Acute Toxicity: LD50>5000 mg/kg, NPIRI

Common Name C.I. Pigment Red 53 Barium

Structure:



Chemical Name Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl) azo] -4-methyl-barium salt

Melting Point 380-390 NPIRI\ 330 °C Company supplied data
Boiling Point: Solid
Density 13.7 to 17.5 Pounds Per U.S. Gallon
Acute Toxicity: LD50 >5000 mg/kg, NPIRI, LD50 > 10,000 mg/kg Company data,
Water Solubility : 2.0 mg/l at 20 °C

SIDS DATA SUMMARY

Physical Chemical Endpoints

Data for physical chemical endpoints was obtained from actual test results reported in reputable publications or from company sponsored tests. Data assessing the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility) for C.I. Pigment Red 49 were also obtained where necessary from estimations using the models within EPIWIN. The data indicate that both substances are stable solids at room temperature, are largely insoluble in octanol and is also insoluble in water .

Environment

For the environment, analysis of Pigment Red 53 indicates that: The highest PEC local of 41.5 µg/l was calculated resulting from paper recycling using a realistic worst case scenario. A pigment red concentration of 3.4 µg/l was measured in one waste water sample from a German deinking plant, resulting in a PEC local of 0.11 µg/l. Since the water solubility of either C.I. Pigment Red 53 or C.I. Pigment Red 49 is about a factor of 50 to 10,000 higher than the estimated PECs for the scenario paper recycling, it can be concluded that C.I. Pigment Red 53 or C.I. Pigment Red 49 represent with high probability a low potential risk to the aquatic environment.

Acute Toxicity

After single oral administration of C.I. Pigment Red 53:1 to rats and mice the compound can be considered to be of low toxicity. The LD50-values determined for both species were > 10000 mg/kg body weight. C.I. Pigment Red 53:1 does not irritate the skin and eyes in respective tests with rabbits and does not show evidence of a sensitizing effect in the modified Maximization Test with guinea pigs. The potential to induce toxicity in mammalian species following acute oral exposure is very low. All types of Pigment Red 49 and C.I. Pigment Red 53 exhibited LD_{50} values of >5,000 mg/kg.

Human Health

Analysis of C.I. Pigment Red 53 (Calcium) indicated that, After repeated oral administration for 90 days in rats C.I. Pigment Red 53:1 led in high dosages (at 3000 ppm and above) to hematological findings (depressed hemoglobin and hematocrit values) and effects on spleen (splenomegaly, haemosiderosis, fibrosis), liver and kidneys (heamosiderosis). Daily administration of C.I. Pigment Red 53:1 for 90 days in mice led to comparable findings. The NOEL for mice was determined as 90 mg/kg bw/day. A 20-week subacute feeding study using 5 male and 5 female weanling Osborne Mendel rats per level and levels of 2 %, 1 %, 0.5 %, 0.25 % and 0 % of D & C Red No. 9 (C.I. Pigment Red 53:1) in the diet produced no mortality but resulted in lower average hemoglobin and hematocrit values. At autopsy splenomegaly was noted in rats on all substance test levels, and liver enlargement was noted at the 1 % and 0.5 % color-feeding levels. 5 groups of 50 3-week old Osborne-Mendle rats were started on a two-year feeding experiment on D & C Red No. 9 at dose levels of 1 %, 0.25 %, 0.05 %, 0.01 % and 0 % (controls). The test substance had no apparent effect on the growth rate, mortality or occurrence of tumors in the test rats. Hemoglobin levels were slightly lowered and abnormal shape of red blood cells were observed in rats on the 1 % and 0.25 % feeding levels (no further information given). At autopsy, survivors on the 1 % feeding level showed moderate splenomegaly and rats on the 0.25 % level showed slight splenomegaly. Histopathologic findings attributable to the color feeding consisted of moderate splenomegaly at 1 %, slight splenomegaly at 0.25 %, and slight bone marrow hyperplasia at both levels. The 1 % feeding level rats also showed slightly increased splenic haemosiderosis and some had splenic infarcts. At 0.05 % and 0.01 % there were no gross or microscopic pathologic changes attributable to D & C Red No. 9 (C.I. Pigment Red 53:1). The No Observed Effect Level (NOEL) was determined as 25 mg/kg bw/day (0.05 % color in the diet).

Carcinogenicity
Animal data:

A peer reviewed published two year chronic toxicity study of C.I. Pigment Red 49 (D &C Red 10) in the rat showed no dose related toxicity.

100 ICR (Swiss Webster derived) mice - 50 males and 50 females - received C.I. Pigment Red 53:1 two times per week for 18 months at the shaven back to an area of approximately 6 cm2. Dosage levels were based on lipstick use determinations made in a group of human female volunteers. Twice each week a 0.1 ml dose containing 1 mg of the dye was applied to the dorsal of each mouse with an automatic syringe and uniformly distributed on the exposed skin with a rubber applicator. Animals that died, those sacrificed moribund and those surviving the 18 months experimental period were necropsied. After termination of the study, tissues were selected for histopathology, sectioned, stained with hematoxylin and eosin and examined by a pathologist. The repeated application of 0.1ml containing 1 % dye did not increase the incidence of neoplasms when compared to the vehicle controls.

A well conducted NTP bioassay of D & C Red No. 9 (C.I. Pigment Red 53:1) in groups of 50 male and female F344 rats and B6C3F1 mice, at dose levels of 0, 1,000 and 3,000 ppm (rats) and 0, 1,000 and 2,000 ppm (mice) for 103 weeks showed no effect on

survival and body weight effect was seen in female mice only.

There were no findings of significance in mice of either sex. In rats there was an increased incidence of splenic sarcoma (mainly fibrosarcoma) in high dose males only. These are tabulated under spleen lesions, splenic capsule and splenic red pulp. This treatment related effect is a consequence of prolonged splenic injury (congestion and fibrosis). There were no splenic sarcomas in low dose males or any of the female groups. There were small increases in neoplastic nodules of the liver in male rats. The only malignant liver tumor occurred in a control rat. It is noted that the incidence of some tumors, lymphomas, leukemia and preputial gland tumors was decreased in treated groups.

In a long term 2-year feeding study with Osborne-Mendel rats there was no increase in tumor incidence up to the highest feeding level of 500 mg C.I. Pigment Red 53:1 per kg body weight (10,000 ppm).

Charles river rats (CD strain) with in utero and lifetime exposure to D & C Red No. 9 (C.I. Pigment Red 53:1) in the diet reveals a small number of highly unusual mesenchymal neoplasms of the spleen. The increased incidence of these tumors was not statistically significant in the dosed animals in this study; however, due to their highly unusual nature and the possibility of tumor origin in nonneoplastic fibrosis it is highly likely that these tumors were compound induced. ICR mice with dermal exposure for 18 months showed no increased evidence of neoplasms. In summary long-term carcinogenicity studies with Osborne Mendel rats and B6C3F1 mice gave no indication of a carcinogenic effect of C.I. Pigment Red 53:1. In the NTP bioassay with fisher F344 rats there was an increased incidence of splenic sarcomas only in one sex (male) and only in the highest dosage group. The development of these tumors as well as the findings with Charles River rats after in-utero and lifetime exposure can probably therefore be attributed to a toxic effect of the substance. Regarding this effect the examiners comment: "The serious non-neoplastic lesions of the spleen in the (male) rats of the highest dosage group suggest a connection between the toxicity of the administered substance and the formation of splenial neoplasms." A statistically significant incidence of splenic sarcoma (0/50, 0/50, 26/48, $P > 0.001$) in male rats fed with high dose levels of C.I. Pigment Red 53:1 is concluded to occur only above a biological threshold level at which the spleen is damaged. Provided low levels of exposure to C.I. Pigment Red 53:1 are maintained, potential risk resulting from use of the pigment is considered to be insignificant. Recommendation: no need for follow-up test

Reproductive Toxicity

Animal data:
The purpose of a 30-months chronic toxicity and potential carcinogenicity study in rats with in utero and lifetime exposure to D & C Red No. 9 (C.I. Pigment Red 53:1) via its incorporation into the basal diets at doses of 0 and 10,000 ppm also was to evaluate the reproductive performance of the F0 generation. Rats of the Charles river CD strain were 35 days of age when treatment was initiated.

After nine weeks of treatment, the animals were mated by pairing for seven days. The effect of test material for the in-utero phase was evaluated via mortality, clinical observations, body weight, food consumption, sex ratio, pup viability data and gross necropsy observations on selected animals. Compound consumption was judged to cause orange discoloration of the animals and their feces and an enlargement of their spleens during the in-utero and chronic phases. The chronic phase revealed non-neoplastic compound related effects which included a significant decrease in the red blood cell parameters (red blood cell count, packed cell volume and hemoglobin percent) and an increase in the reticulocyte count observed after 3, 6, 12, 18 and 24 months of treatment. Compound consumption was judged to be associated with a significant increase in spleen weight, and the following non-neoplastic lesions of the spleen; extramedullary haematopoiesis, congestion, fibrosis, haemosiderosis, mesothelial hyperplasia, mesothelial cystformation, capsular fibrosis and multifocal cellular proliferations in the capsule. The accumulation of haemsiderin in some other organs of the treated rats also suggest a compound-related effect. The combination of decreased red cell parameters, reticulocytosis and haemosiderosis supports the hypothesis that there was a compound related decreased erythrocyte survival and a haematopoietic response to that decreased red cell survival.

Conclusion

All endpoints have been satisfied with data, on C. I. Pigment Red 49 or through the use of structural surrogates and estimates, which are of sufficient quality to conclude that no additional testing is needed. Since these substances are extremely stable and insoluble in

water, ink formulations or other uses, such as paints and plastic formulations, and since these substances are encapsulated in these applications, exposure to these products in use is extremely limited.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance (3) and the systematic approach described by Klimisch *et al.* (4). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation (5). The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

1. Reliable without Restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. Not Reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. Not Assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, Version 3.10, Syracuse Research Corporation, Syracuse, New York.

2. US EPA. (1999). The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.

3. USEPA (1998). 3.4 Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.

4. Klimisch, H.-J., Andreae, M., and Tillmann, U. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regul. Toxicol. Pharmacol.* 25:1-5.

5. USEPA. 1999. Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.

I. General Information

CAS Number: C.I. Pigment Red 49 (Barium) (CAS NO.:1103-38-4)

Name: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium

II. Physical-Chemical Data

A1. Melting Point

Test Substance

Test substance: Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl) azo]-4-methyl-barium salt (R53)

Remarks:

Method

Method: Measured

Remarks:

Results

Melting point value:

Remarks: 330 °C

References Unpublished company data reliable with restrictions. Hoechst AG (1992) Unveroeffenlichte Untersuchung Der Abt. Analytisches Laboratorium (17.11.1992)

Other

Data is consistent with melting points for the class of pigments and other available measurements

A2. Melting Point

Test Substance

Test substance: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl) azo]-,barium R 49)

Remarks:

Method Estimation

Method:

Remarks:

Results

Melting point value: 349.84 °C

Remarks:

References MPBPWIN v1.40 in EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

Other

Data is consistent with melting points for the class of pigments and other available measurements.

B. Boiling Point

Test Substance

Test substance: SOLID N/A
Remarks:

Method

Method:
Remarks:

Results

Boiling point value:
Remarks:

References

Other

C1. Vapor Pressure

Test Substance

Test substance: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium R 49)
Remarks:

Method

Method: Estimation
Remarks: Modified Grain method

Results

Vapor pressure value: 4.62 E-015 mm Hg
Temperature:

Remarks:

References

MPBPWIN v1.40 in EPIWIN v3.10, Syracuse Research Corporation, Syracuse, New York

Other

D. Partition Coefficient

Test Substance

Test substance: Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt R 53)

Remarks:

Method

Method: Estimated

Remarks:

Results

Log P_{OW}: -.56

Remarks:

References

Hoechst AG (1997) : Unveroeffentlichte Untersuchung Pigmentanalytik (25.02.1997) SIDS Dossier C.I. Pigment Red 53

Other

E. Water Solubility

Test Substance

Test substance: Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt R 53)

Remarks:

Method

Method:

Remarks: Estimated

Results

Value: 2 mg/L

Temperature: 25 °C

Description:

Remarks: Very Low Solubility

References

Hoechst AG (1993):Unveroeffentlichte Untersuchung (93.0358)
SIDS Dossier, C.I. Pigment Red 53

Other

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance

Test substance: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium R 49)

Remarks:

Method

Method: Estimate

Test type: Water\sunlight

Remarks:

Results

Temperature:

Degradation Rate

18.6 E-12

: Half-life

Ozone reaction: 6.9 Hours **(or not readily degradable, estimation not possible)**

Remarks:

Conclusions

References

AopWin v1.90 in EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

Other

A2. Photodegradation

Test substance: Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt R 53)

Remarks:

Method

Method: Estimation

Test type: Water

Remarks:

Results

Temperature:

Hydroxyl radicals reaction

OH Rate constant:

Half-life estimation not possible

Ozone reaction:

Remarks:

Conclusions

References

Hoechst AG (1991):Einstufungsbegrundung TA-Luft der Abt.UCV (19.07.1991) IUCLID dataset C.I. Pigment Red 53

Other

B. Stability in Water

Test Substance

Test substance: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium R 49)

Remarks:

Method

Method:

Test type: Estimation

GLP: abiotic hydrolysis

Remarks: Yes

Results

Half-life: Hydrolysis rate cannot be estimated

Percent hydrolyzed in 5 days (120 hs) at 50 °C :

Remarks:

Conclusions

Data Quality

Remarks:

References EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

Other

C. Biodegradation

Test Substance

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt R 53)
Remarks:	

Method

Method:	OECD 301C
Test type:	MITI 1 and Zahn Wellens Inherent biodegration
GLP:	Yes
Year:	(1992)
Remarks:	No biodegradation (MITI 1 Japanese standard activated sludge)

Results

Results:	33% eliminated after 21 days in Zahn Wellens test, 10 % of elimination due to adsorption onto the sludge
Remarks:	

Conclusions

Data Quality

Remarks:	This is a well-documented study.

References

Ministry of International Trade and Industry (MITI) (1992) Biodegradation and Bioaccumulation data for existing chemicals based on the Chemical Substances Control Law, Japan Chemicals Inspection and Testing Institute; Japan Chemical Industry Ecology - Toxicology and Information Center 14-19, 5-43, See also IUCLID dataset and SIDS DOSSIER C.I. Pigment Red 53.

Other

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Test substance: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium

Remarks: R 49)

Method

Test type:

Model used: Estimation

Level III Fugacity Model; EPIWIN:EQC from Syracuse Research

Remarks: Corporation

Results

Model data and results:

	Distribution (%)
Air	.0791
Water	2.06
Soil	38.7
Sediment	59.2

Remarks: Since no experimental values were available the physical chemical values utilized in this model were default parameters from within EPIWIN.

Conclusions

References

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15(9)**, 1618-1626 and 1627-1637.

Other

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt R 53)
Remarks:	

Method

Method:	Method 84/449/EEC
Test type:	Static system
GLP:	Yes
Year:	1982
Species/strain:	Brachydanio rerio
Analytical monitoring:	
Exposure period:	96-Hour
Remarks:	A group of 10 fishes were exposed to 5 nominal concentrations (17.1-180), DMSO Control(.5mg/l)and laboratory water control

Results

Nominal concentration:	
Measured concentration:	
Endpoint value:	96-hour LC_{50} >500mg/L
Biological observations:	
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References

Hoechst AG (1982) :Unveroeffentlichte Untersuchung (82.0250). See also EUCLID Dataset C.I. Pigment Red 53 and SIDS Dossier C.I. Pigment Red 53

Other

A2. Acute Toxicity to Fish

Test Substance

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt
Remarks:	

Method

Method:	
Test type:	Semistatic system
GLP:	Yes
Year:	1982
Species/strain:	Oryzias latipes (Orange Killifish)
Analytical monitoring:	
Exposure period:	48-Hour
Remarks:	

Results

Nominal concentration:	
Measured concentration:	48 hour LC_{50} >500 mg/L
Endpoint value:	
Biological observations:	
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable without restrictions
Remarks:	

References

Hoechst AG (1982) :Unveroeffentlichte Untersuchung (82.0250). See also EUCLID Dataset C.I. Pigment Red 53 and SIDS Dossier C.I. Pigment Red 53

Other

B. Acute Toxicity to Aquatic InvertebratesTest Substance

Test substance:

Remarks: Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt R 53)

Method

Method: OECD 202.
Test type: Saturated solution
GLP: Yes
Year: 1993
Species/strain: Daphnid (*Daphnia magna*)
Analytical monitoring:
Exposure period:
Remarks:

Results

Nominal concentration:
Measured concentration:
Endpoint value: Saturated solution

Reproduction: 48 -hour EC_{50} >2mg/l

Biological observations:

Statistical methods:

Remarks:

Conclusions

Data Quality

Reliability: Reliable without restriction
Remarks: This was a well-documented OECD guideline study.

References

Hoechst AG (1993):Unveroeffentlichte Untersuchung (93.0358)
See also EUCLID dataset and SIDS Dossier, C.I. Pigment Red 53

Other

C. **Toxicity to Aquatic Plants**

Test Substance

Test substance:	1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium ® 49)
Remarks:	

Method

Method:	Estimation
Test type:	
GLP:	
Year:	
Species/strain:	
Endpoint basis:	
Exposure period:	
Analytical procedures:	
Remarks:	The conduction of an algae test with C.I. Pigment Red 49 is problematic as the substance leads to a strong coloring of the test solution and therefore to a reduction of light intensity. Therefore, the assessment is made on the basis of the above short term tests and computer model estimation.

Results

Nominal concentration:	
Measured concentration:	
Endpoint value:	
NOEC:	
Biological observations:	
Was control response satisfactory:	EC 50, 96 Hour .038 mg/L
Statistical Methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	
Remarks:	

References reliable with restriction

Other

EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

V. Toxicological Data

A. Acute Toxicity

Test Substance

Test substance:	1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium ® 49)
Remarks:	Purity was unknown

Method

Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No (Pre-GLP)
Year:	1968
Species/strain:	Rat/unknown
Route of exposure:	Oral gavage
Dose levels:	Unknown
Remarks:	

Results

Value:	LD_{50} = >5,000 mg/kg.
Deaths at each dose:	
Remarks:	

Conclusions Material would be considered as not toxic.

Data Quality

Reliability:	Reliable with restrictions
Remarks:	The study was conducted quite some time ago and hence many study details are missing from the report and not available. However, basic data are given and results are consistent with other data for pigments of this class.

References

Mone J.G. 1968, Federation Series on Coating Technology, Unit 9 Organic Pigments, Federation of Societies for Paint Technology, Philadelphia, PA 19107.

Other

Acute toxicity

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt ® 53)
Remarks:	Purity was unknown

Method

Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No (Pre-GLP)
Year:	1977
Species/strain:	Rat and mouse
Route of exposure:	Oral gavage
Dose levels:	Unknown
Remarks:	

Results

Value:	LD_{50} = >10,000 mg/kg.
Deaths at each dose:	
Remarks:	

Conclusions Material would be considered as not toxic.

Data Quality

Reliability:	Reliable with restrictions
Remarks:	

References Hoechst AG (1977):Unveroffentl. Unters (Ber.-Nr. 77.0525. See also EUCLID Dataset and SIDS DOSSIER C.I. Pigment Red 53

Other

Acute Inhalation Toxicity LC50 > 4.13 mg/l, 1993, GLP study, Hoechst AG (1977):Unveroffentl. Unters (Ber.-Nr. 93.0427)

Repeated Dose Toxicity Test

Substance

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt (R53)
Remarks:	

Method

Method:	
Test type:	Repeated subchronic dose
GLP:	Unknown
Year:	1982
Species/strain:	Rat Male and Female, Mice male and Female
Route of exposure:	Gavage
Duration of test:	91 days
Exposure levels:	Rats 0. 3000,6,000, 12,500, 25,000, or 50,000 ppm Mice 0,600,12,500,2,500,5,000, 10,000
Sex:	Male and Female Rats and Mice
Exposure period:	91 days
Post-exposure observation	
Remarks:	

Results

NOAEL (NOEL):

90 mg/kg mice, 25 mg/kg rats
After repeated oral administration for 90 days in rats pigment red 53:1 led in high dosages (at 3000 ppm and above) to hematological findings (depressed hemoglobin and hematocrit values) and effects on spleen (splenomegaly, haemosiderosis, fibrosis), liver and kidneys (heamosiderosis). Daily administration of pigment red 53:1 for 90 days in mice led to comparable findings. The NOEL for mice was determined as 90 mg/kg bw/day.

Conclusions Test substance is not significantly toxic

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References: Carcinogenesis Bioassay of D & C Red No. 9 In F344 Rats and B6C3F1 Mice National Toxicology Program Technical Report Series No. 225. **See also EUCLID** dataset C.I. Pigment Red 53 for other studies conclusions consistent.

Other

C. Genetic Toxicity - Mutation

Test Substance

Test substances: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium **and** Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt ® 49 and R 53)

Remarks:

Method

Method:	In Vitro Mutagenicity
Test type:	Ames
GLP:	Unknown
Year:	Unknown
Species/strain:	Salmonella typhimurium
Metabolic activation:	Yes, barium salt (and manganese salt)
Concentration tested:	
Remarks:	

Results

Result:	Negative
Cytotoxic concentration:	
Precipitation concentration:	
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable with restrictions
Remarks:	

References

Brown, J.P., P.S. Dietrich & C. M. Bakner, 1979, "Mutagenicity testing of some drug and cosmetic dye lakes with salmonella/mammalian microsome assay," Mutat. Res., 66, 181-185., Muzzall, J.M. & W.L.Cook, 1979 "Mutagenicity test of dyes used in cosmetics with salmonella/ mammalian microsome test", Mutat. Res., 67,1-8 ,Milvy, P. & K. Kay 1978 "Mutagenicity of 19 major graphic arts and printing dyes, J. Toxcol. Environ. Health, 4, 31-6 NPIRI Raw Materials Handbook, 2000

C. Genetic Toxicity - Mutation

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt
Remarks:	® 53)

Method

Method:	OECD 471
Test type:	Ames
GLP:	Yes
Year:	1985
Species/strain:	Salmonella typhimurium
Metabolic activation:	With and without
Concentration tested:	4 - 5000 ug/plate with and without activation
Remarks:	

Results

Result:	Negative in all bacterial strains with and without activation
Cytotoxic concentration:	
Precipitation concentration:	
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability: Reliable without restriction Remarks:

References Hoechst AG (1977):Unveroffentl. Unters (Ber.-Nr. 85.0974). See also EUCLID dataset and SIDS DOSSIER C.I. Pigment Red 53

Other

D. Genetic Toxicity – Chromosomal Aberrations

Test Substance

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt ® 53)
Remarks:	

Method

Method:	OECD 473
Test type:	Cytogenetics Assay
GLP:	Yes
Year:	1989
Species/strain:	Chinese Hamster CHL Cells
Exposure period:	
Remarks:	

Results

Result:	Negative
Genotoxic effects:	Negative
Concentration tested	30, 150,300 ug/ml
Statistical methods:	
Remarks:	

Conclusions Not mutagenic

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References Hoechst AG (1977): Unveroffentl. Unters (Ber.-Nr. 89.1443). See also EUCLID dataset and SIDS DOSSIER C.I. Pigment Red 53

Other

E. Developmental Toxicity

Test Substance See 30 Month toxicity study below

Test substance:

Remarks:

Method

Method:

GLP:

Year:

Species/strain:

Sex:

Route of exposure:

Exposure levels:

Actual doses received:

Exposure period:

Duration of test:

Remarks:

Results

Maternal toxicity NOEL:

NOEL for teratogenicity:

NOEL for fetotoxicity:

Parental toxic responses:

Fetal toxic responses dose:

Statistical Methods:

Remarks:

Conclusions

Data Quality

Reliability:

Remarks:

References

Other

F. Toxicity to Reproduction

Test Substance

Test substance:	Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt
Remarks:	

Method

Method:	30 month Chronic Toxicity and Potential Carcinogenicity Study in Rats with In Utero and Lifetime Exposure to D & C Red No. 9 in the Diet
GLP:	no
Year:	1981
Species/strain:Sex:	Rat male and female
Route of exposure:	gavage
Exposure levels:	0, 10,000 mg/kg
Exposure period:	30 Months
Duration of test:	
Remarks:	

Results

Maternal toxicity NOEL:	NOEL< 10,000 ppm
Parental toxic responses:	NOEL >10,000 ppm
Fetal toxic responses dose:	NOEL >10,000 ppm (F1)
Statistical Methods:	
Remarks:	The purpose of a 30-months chronic toxicity and potential carcinogenicity study in rats with in utero and lifetime exposure to D & C Red No. 9 (pigment red 53:1) via its incorporation into the basal diets at doses of 0 and 10,000 ppm also was to evaluate the reproductive performance of the F0 generation. Rats of the Charles river CD strain were 35 days of age when treatment was initiated. After nine weeks of treatment, the animals were mated by pairing for seven days. The effect of test material for the in-utero phase was evaluated via mortality, clinical observations, body weight, food consumption, sex ratio, pup viability data and gross necropsy observations on selected animals. .

Conclusions

Data Quality

Reliability:	There was no evidence for an impairment of reproductive functions in animals
Remarks:	

References

Other Reliable with restriction, this is a well documented study.

Litton Bionetics Study for the Cosmetic, Toiletry and Fragrance Association, Inc. LBI Project Number 20832, June 1981,

Acute toxicity

Test substance:	1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium **and** Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt
Remarks:	

Method

Method:	Irritation to the rabbit eye
Test type:	eye irritation
GLP:	unknown
Year:	
Species/strain:	rabbit
Route of exposure:	
Dose levels:	
Remarks:	

Results

Value:	negative
Deaths at each dose:	
Remarks:	

Conclusions

Data Quality

Reliability:	un-assignable
Remarks:	

References **Company data**

Other

Acute toxicity

Test substance:	1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium **and** Benzenesulfonic acid, 5 chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-barium salt
Remarks:	

Method

Method:	Skin irritation to the rabbit
Test type:	Skin irritation
GLP:	unknown
Year:	
Species/strain:	rabbit
Route of exposure:	
Dose levels:	
Remarks:	

Results

Value:	negative
Deaths at each dose:	
Remarks:	

Conclusions

Data Quality

Reliability:	Published peer review study
Remarks:	

References **Company data**

Other

Chronic Dose Toxicity Test Substance

Test substance: 1-Naphthalenesulfonic acid, 2[(2-hydroxy-1-(Naphthalenyl)azo]-,barium

Method

Method: Chronic Toxicity
Test type: Repeated oral dose
GLP: unknown
Year: 1963
Species/strain: Rat
Route of exposure: Oral gavage
Duration of test: two years
Exposure levels:
Sex:
Exposure period:
Post-exposure observation period:
Remarks:

Results

NOAEL (NOEL):

No cancerous response. No toxicity or mortality as a result of exposure

Conclusions

Data Quality

Reliability: un-assignable
Remarks:

References

Davis, K.J. & O.G. Fitzhugh, 1963, "Pathologic changes noted in rats fed D & C Red No. 10 for two years", Toxicol. Appl. Pharmacol.,4, 200-205

Other